Remarks/Arguments:

Applicant would like to thank the Examiner for taking the time to discuss the 35 USC §112, first paragraph new matter and 35 USC §103 rejections during a telephonic interview held on April 8, 2008.

Claim Status

Claims 33, 34 and 44-47 are pending in this application.

35 USC 112, first paragraph

Claims 33, 34 and 44-47 are rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. The claims are alleged to contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner states that the last step (h), drawn to a correlation of the apoptosis inhibition results obtained from the transfected cells (d) and the tissue biopsy (h), is new matter. Applicants respectfully traverse.

Applicants respectfully submit that correlating the results of *in vitro* and *in vivo* testing is described in the specification as originally filed. At Page 19, Line 21 through Page 20, Line 20, the specification discloses specific *in vitro* testing, the results of which are used to design and direct further *in vivo* testing, such as animal models or clinical trials. The disclosed *in vitro* tests are used to access the effectiveness of neuronal protection by JNK or MLK inhibitors against excitotoxicity stimuli by the pre-treatment of HN33 cell with the identified JNK or MLK inhibitors prior to stimulation with glutamate, or other neurotoxins. (Page 19, Lines 25-28) "The IC_{50} of each inhibitor is a very important value for designing further study of the effectiveness in different animal models and for directing clinical trials of these inhibitors." (Page 20, Lines 28-20).

For at least this reason, Applicants respectively submit that the specification sufficiently describes with reasonable clarity to those skilled in the art that, as of the filing date, the Applicants were in possession of the invention. Therefore, Applicant respectfully request that this rejection be withdrawn.

35 USC 103(a)

Claims 33, 34, 44 and 47 are rejected under 35 USC § 103(a) as being unpatentable over U.S. Patent No. 6,943,000 to Davis et al ("Davis et al.") in view of Reynolds et al., J. Neurochem, Vol. 68, No. 4, 1997 ("Reynolds et al.). Applicant respectfully traverses.

Applicants respectfully bring to the Examiner's attention the prosecution history of Applicant's related U.S. Patent Application Serial No. 10/360,463 which has matured into U.S. Patent No. 7,264,942. During the prosecution of 10/360,463, Examiner Marianne Allen raised similar 35 USC § 103(a) rejections based Davis et al., alone and in combination. These rejections were overcome by claim amendments and argument. The same claim amendments and argument are presented herein.

The action states that Davis et al. disclose *in vitro* and *in vivo* methods for screening inhibitors of JNK3 for diseases involving excitotoxicity. The action then states that Davis et al. meet steps (a) and (b) of claim 33 because Davis et al. disclose incubating a test compound with a JNK and its substrate.

While claims 33, 34, 44 and 47 are directed to screening for inhibitors of JNK and its claimed isoforms, there is no motivation presented by Davis et al. to incorporate the claimed steps of this invention. Specifically, as set forth in claim 33, step (c) requires the contacting step to be conducted in neuronal cells either transfected with mutated protein, specifically polyglutamine stretch-expanded huntingtin or C-terminal 100 amino acids of amyloid precursor protein, or treated with a neurotoxin to induce apoptosis. With regard to testing candidate inhibitory compounds, Davis et al. alludes to such testing by broadly stating, "[c]andidate inhibitory compounds can be tested further in cell or tissue cultures as well as animal models." (see Davis et al., column 10, lines 11-13). Davis et al. then discloses a single *in vitro* assay for testing such candidate compounds prior to testing or applying such compound *in vivo*. The disclosed *in vitro* assay is directed to measurement of cell lysate protein interactions (see column 10, lines 21-46). There is no disclosure or suggestion in Davis et al. to use transfected neuronal cells, or cells treated with neurotoxin for the *in vitro* testing prior to *in vivo* testing or application. Further, Davis et al. express no desire or motivation to use an alternative *in vitro* assay to the

cell lysate assay disclosed therein, let alone the specific *in vitro* assays set forth in step (c) of claim 44.

In view of the position set forth above, Applicant respectfully requests that rejection of claims 33, 34, 44 and 47 under 35 USC § 103(a) as being unpatentable over Davis et al. in view of Reynolds et al. be withdrawn.

Claims 33, 34, 44, 46 and 47 are rejected under 35 USC 103(a) as being unpatentable over Davis et al. in view of Reynolds et al., as applied to claims 33, 34, 44 and 47, in further view of Liu (1997) ("Liu et al."). Applicant respectfully traverses.

Liu et al. is cited for teaching that TUNEL and staining of cells with Hoechst 33342 is a common alternative to determine neuron apoptosis (see Office Action mailed 6-14-05). Applicant notes, however, that Liu et al. do not provide the elements missing from claim 33 from which the remaining claims depend. As such, Liu et al. does not, when combined with Davis et al and Reynolds et al., render the claims obvious. Applicant respectfully requests that this rejection be withdrawn.

Claims 33, 34, 44, 45 and 47 are rejected under 35 USC 103(a) as being unpatentable over Davis et al. in view of Reynolds et al., as applied to claims 33, 34, 44 and 47, in further view of Gnegy et al. (1976) ("Gnegy et al."). Applicant respectfully traverses.

Gnegy et al. is cited for teaching that *in vitro* and *in vivo* experiments were used to verify that phosphodiesterase protein activator (PDEA) is not the phosphorylation substrate of cAMP-dependant protein kinase. (see Office Action dated 2-2-06). Gnegy et al. however, do not provide the elements missing from amended claim 33, specifically, Gnegy et al. do not teach or suggest at least the specific step (c) of claim 33 which requires the contacting step to be conducted in neuronal cells either transfected with mutated protein, specifically polyglutamine stretch-expanded huntingtin or C-terminal 100 amino acids of amyloid precursor protein, or treated with a neurotoxin to induce apoptosis. As such, Gnegy et al., when combined with Davis et al and Reynolds et al., does not render the claims obvious. Applicant respectfully requests that this rejection be withdrawn.

Conclusion

The foregoing is believed to be fully responsive to the office action dated January 17, 2008. The embodiments presented are believed to be allowable over the prior art of record. Consideration and allowance of the claims is respectfully requested.

If the Examiner believes that a telephone conference with Applicants' attorneys would be advantageous to the disposition of this case, the Examiner is cordially requested to telephone the undersigned. If the Examiner has any questions in connection with this paper, or otherwise if it would facilitate the examination of this application, please call the undersigned at the telephone number below.

In the event that any fee has been inadvertently overlooked and is required, the Commissioner is hereby authorized to charge any required fee or credit any overpayment to **Deposit Account No. 50-3570**.

Respectfully submitted,

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